



REMARKS

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Applicants respectfully request that Group V, claims 9-10, drawn to a method for screening compounds that disrupt transcriptional repression by determining the binding of a protein to a DNA in the presence of the candidate compound, be recombined with the elected claims 11-14 of Group VI for examination. Applicants would like to point out that claims 13-14 were omitted from the Restriction Requirement and assume, as these claims are dependent on claim 11, that they belong with Group VI claims.

Applicants disagree that the methods of Group V and VI are materially different ~~is~~ a significant way. Furthermore, Applicants submit that a search of Group V and VI is coextensive in so far that both Group V and VI are methods of screening for compounds that disrupt transcriptional repression of a gene containing a Hox DNA binding element. The compounds in both Groups V and VI have the identical classification and perform the same function, i.e., they affect the interaction of a Smad6/Hoxc-8 protein complex with the Hox DNA binding element. Group V determines the degree to which a compound interrupts

transcriptional repression of the gene by determining the amount of binding by the Smad6/Hoxc-8 protein complex to the Hox DNA binding element in gene, i.e., less binding correlates with less repression. In Group VI determination of the level of gene transcription indicates the efficacy of a compound, and this can be the same compound as in Group V, in interrupting transcriptional repression of the gene.

Regardless whether the screening method of Group V or Group VI is employed, what is key in either method is that Smad6, acting as a corepressor with Hoxc-8, forms a complex with Hoxc-8 which binds to the Hox DNA binding element in the gene thereby repressing transcription of the gene and that an efficacious compound will disrupt the Smad6/Hoxc protein complex binding to the binding element in the gene. Assaying for protein binding on the gene by those methods recited in claim 10 or for levels of gene transcription, including those methods disclosed in claim 12, are standard routine procedures in the art and would be inherent in any prior art disclosed.

Because the level of gene transcription is dependent on the level of Smad6/Hoxc-8 binding to the Hox DNA binding element in the gene and because the compounds screened for in Groups V and

VI have the same classification, Applicants submit that a search of the prior art for Group VI, claims 11-14, would necessarily disclose that prior art for Group V, claims 9-10. Thus, it would not unduly burden the Examiner to perform a search of Group V, claims 9-10 and Group VI, claims 11-14. Accordingly, Applicant respectfully requests that the claims 9-10 be examined with claims 11-14.

Applicants believe no fees are due, however, should this be in error, please debit any fees that may be required from Deposit Account No. 07-1185, on which the undersigned is allowed to draw.

Respectfully submitted,



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